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Antitumor effect of vaccinia virus in glioma model.

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The ability of certain viruses to lyse cancer cells suggests that they may have potential as oncolytic agents. We investigated the effect of vaccinia virus (VV) and its recombinant derivatives (recVV2, rVV-p53) on growth of C6 rat glioma cells that form fast growing tumors in athymic nude mice. VV effectively infected C6 cells in vitro, inducing high level of foreign gene expression. Most of C6 cells infected in vitro with rVV-p53 expressing the tumor suppressor p53 protein showed apoptosis specific morphological changes in DAPI-stained nuclei and DNA fragmentation pattern on gel electrophoresis; infection with VV induced low level of cell apoptosis. In an ex vivo experiment, VV-infected C6 cells were implanted s.c. in athymic nude mice and tumor development was monitored. In contrast to the control PBS group, most of mice implanted with infected cells remained tumor free until the end of the observation period. In an in vivo experiment, injection of VV or rVV-p53 after the C6 cells had been implanted in nude mice induced effective inhibition of tumor growth in comparison with control PBS groups. The oncolytic effect was greater with rVV-p53, apparently due to overexpressed p53 and p53-mediated cell apoptosis. In study of virus virulence we did not observe disease symptoms in athymic mice infected with a high dose of VV. Experimental results indicate that vaccinia virus itself and vaccinia-mediated delivery of therapeutic genes represent novel potential strategies for tumor therapy.

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